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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Hiatt, et al.

Title: IMMUNOGLOBIN BINDING PROTEIN ARRAYS IN EUKARYOTIC CELLS

Appl. No.: 10/783,950

Filing Date: 02/19/2004

Examiner: Wessendorf, Teresa D.

Art Unit: 1639

DECLARATION OF ANDREW HIATT, Ph.D, UNDER 37 C.F.R. § 1.132

I, Andrew Hiatt, hereby declare that:

1. I was educated at the University of Vermont where I received a B.A. degree and at Columbia University where I received a Ph.D. degree. I was a postdoctoral fellow in the Delbruck Laboratory at the Cold Spring Harbor Research Laboratory and an assistant professor at the Scripps Clinic and Research Foundation. I have conducted research in plant biotechnology for over 20 years and am the author or co-author of over 30 published scientific articles in biomedical science. A brief summary of my accomplishments and a recent copy of my Curriculum Vitae is attached as APPENDIX 1. I was a founder and the chief scientific officer of Epicyte Pharmaceutical, Inc., a company focused on technology for expressing antibody products in plants. I am currently the chief scientific officer of Mapp Pharmaceutical, Inc. and a scientific consultant to Biolex, Inc., assignee of the above-identified application. I am named as a co-inventor of the above-identified patent application.

2. I understand that the Examiner has rejected claims from the above-referenced patent application as allegedly failing to meet the written description requirement. The Examiner bases the rejection on an alleged unpredictability in the art for transfecting plants with foreign genes and cites as support a reference of mine (Hiatt et al., FEBS, vol. 307, p. 71-75 (1992)) and one by Choi, et al. (Nucleic Acids Research,

vol. 28, e19 (2000)). In my opinion, the Examiner's reliance on these references to demonstrate unpredictability of the art is misplaced. I will explain my position by addressing each reference separately.

I. Hiatt et al. Reference

3. The Examiner refers only to two sentences of my publication from May 1992, where I advised that not all plants are amenable to foreign gene transfection and that one should express only one immunoglobulin in each vector and to transform separate plants with individual heavy and light chain expressing vectors. This advice, from 1992, which is only a few years after my breakthrough discovery that antibodies could even be produced in plants, was no longer relevant when my patent application was filed eight years later in May of 2000. I cite in support an exemplary review article by Giddings, et al. in Nature Biotechnology, vol. 18, p. 1151-56 (2000) (copy provided), which refers to my first publication on antibody expression in 1989 and concludes that "a considerable amount of effort has been invested in developing plants for antibody (or "plantibody") production" since my discovery. Giddings cites to various references describing techniques for transfecting genes into a wide variety of plants. Thus, it is readily apparent that the ability of using plants to express foreign genes has increased dramatically in the eight years since my 1992 reference. In fact, I predicted that this very thing was going to happen in my 1992 article in a sentence that was not mentioned by the Examiner but is found bridging the two sentences quoted by the Examiner. The Examiner's quoted text and the missing sentence between that refers to the rapidly developing field is shown.

> Not all plants are amenable to the manipulations required for the stable introduction of foreign DNA. Tobacco is the most commonly used plant, since it is easily transformed and regenerated. **However, a tremendous effort is being made in various laboratories to perfect transformation techniques for common crop plants such as corn, soybean, alfalfa and rice.**
>
> As plant expression vectors are generally large already [28], and contain only one polylinker region, it is probably wise to express only one immunoglobulin in each vector and to transform separate plants with individual heavy and light chain expressing vectors.

Hiatt et al., p. 71, col. 2, line 21 to p. 72, col. 1, line 2 (emphasis added). The Examiner's emphasis on my 1992 publication while ignoring the statement of currently developing work indicates a failure to properly consider the published literature.

II. Choi, et al. Reference

4. The Examiner also cites to the Choi et al. reference to allege unpredictability in the art. However, Choi et al. relates to methods not relevant to my invention. Choi et al. describes methods for site-specific plant transformation of large DNA inserts used in gene expression experiments. In contrast, my invention is directed to creating a library of antibody genes to find new antibody specificities. While the Choi et al. method is appropriate for large segments of DNA (up to 350 kb), my method can readily use much smaller fragments (~5-7 kb) for which traditional transfection methods are more than adequate. Choi et al. does not negate the fact that traditional methods work for the present invention, but instead provides an improvement to traditional transfection methods useful in gene expression experiments that require single copy, site-directed insertions of large DNA fragments. Because Choi et al. deals with special needs not applicable to my invention, Choi et al. is not relevant to judge the predictability of the methods of gene transfection that underlie my invention.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the captioned patent application or any patent issued therefrom.

7/17/06
Date

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